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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,844	08/06/2001	Shujath M. Ali	DEX-0176	7509
26259	7590	07/13/2005		
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			EXAMINER YU, MISOOK	
			ART UNIT 1642	PAPER NUMBER

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/787,844

Applicant(s)

ALI ET AL.

Examiner

MISOOK YU, Ph.D

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9,13-15,17-19 and 21-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8,9,13-15,17-19 and 21-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/16/05</u> | 6) <input checked="" type="checkbox"/> Other: <u>Exhibit A (sequence alignment)</u> . |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/16/2005, and 4/15/2005 has been entered.

Claims 8, 9, 13-15, 17-19, and 21-33 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of objection to the claims.

Claim Objection, Newly Objected

Since claims 13, 17, 21, 22-24, 26, and 27 depend on claim 8 reciting "Pro104" limited to SEQ ID NO: 2, all of the limitations in the rejected dependent claims are the inherent characteristics of SEQ ID NO: 2, thus not further limiting the base claims.

Claim Rejections - 35 USC § 112, Maintained

Claims 8, 9, and 13-15, 17-19, and 21-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reason of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is based on the Office's interpretation of the nature of the invention as drawn to a method of imaging of a gynecologic cancer using an monoclonal or polyclonal antibody which specifically binds to SEQ ID NO: 2 (claims 8, 13), wherein said antibody is labeled (claim 9), or method of delivering a derivatized antibody (the specification at page 7 line 14, appears to limit "derivatized" as attaching cytotoxic agent or other art-known agents to an antibody that binds to SEQ ID NO: 2), which specifically binds to SEQ ID NO:2, to a gynecologic cancer cell in vivo (claims 14, 15, 17), or delivering said derivatized antibody to a gynecologic tumor in vivo (Claims 18, 19, 21), wherein new claims 22-27 characterizes that the protein of the base claims to be protease with active domains, or SEQ ID NO:2, wherein the new claims 28-33 specifies various gynecologic cancer.

Applicant argues that instant Pro104 is same as testisin that are highly expressed in ovarian cancers as disclosed by Tang et al., (2005, Cancer Res., vol. 65, pages 868-78, IDS filed on 03/16/2005), and also as disclosed in Papkoff et al (IDS filed on 03/16/2005).

Applicant's arguments and data shown in the poster presentation of Papkoff et al., and the post-filing publication of Tang et al., have been fully considered, but unpersuasive for the following reasons. First, during the prosecution history, the limitation "Pro104" in the instant claims is determined to be limited to the instant SEQ ID NO: 2 protein. See the Office action mailed on 04/21/2004, and applicant's subsequent response, as well as the interpretation of the claims. The specification as originally filed does not reasonably communicates that the protein known in the art, as "testisin" is

same as the instantly claimed Pro104. The attached sequence alignment aligning the instant SEQ ID NO: 2 against what is the protein known as testisin in the art (Exhibit A) demonstrate that instant SEQ ID NO: 2 is not same as testisin. Therefore, the argument with Tang et al., is not germane to the instantly claimed invention.

As for argument with Papkoff et al., Papkoff et al., discloses the Pro104 is over-expressed in ovarian cancer. However, Papkoff et al., do not establish whether Pro104 is same as the instant SEQ ID NO:2. In fact, one of the figure in the poster, top in the 2nd column appears to indicate that Pro104 in Papkoff et al., is testisin, not instant SEQ ID NO:2. In addition, Papkoff et al., do not establish that whether one could image gynecologic cancers using polyclonal or monoclonal antibody specifically binding to the instant SEQ ID NO:2 encoded by instant SEQ ID NO:1. Papkoff et al., teach that detection of overexpression of Pro104 (testisin) in ovarian cancer tissue samples as compared to normal ovarian tissue.

As stated before in the two previous Office actions, Aloj et al., (2002, Biopolymers. Vol. 66, pages 370-80) teach that in order to target specific molecules inside the body using radiopharmaceuticals such as a radioisotope-labeled antibody, several parameters have to be considered: (1) the target protein should be over-expressed in cancer to be imaged; (2) a radiopharmaceutical should be tested to see whether said radiopharmaceutical specifically binds to the *in vivo* target *in vivo*; (3) how the unbound radiopharmaceutical is cleared for minimizing unwanted high background (note the abstract, and pages 372-373). The instant specification has failed to teach with a reasonable certainty that the protein encoded by SEQ ID NO:1 is a gynecologic

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cancer antigen while the art (see Hooper et al., above) suggests that the protein encoded by SEQ ID NO:1 is a tumor suppressor. Low et al., (1995, Radiology, vol. 195, pages 391-400) also teach that in order to image an ovarian cancer (a species of a gynecologic cancer), selection of an antibody that specially binds to an ovarian cancer-associated antigen, is the first necessary step (see page 391 middle column; the authors selected an antibody targeting Tag-72, a previously known ovarian cancer antigen). Low et al., further teach accuracy of imaging using an antibody directed to a cancer antigen has to be evaluated against other known cancer detection methods such as histology or pathology (note page 393 under the heading "Pathologic Proof", and Table 3 at page 396). Likewise, Krag et al., (1993, Arch. Surg. Vol. 128, pages 819-23) teach method of imaging an ovarian cancer using a radio-labeled (i.e. indium 111-labeled) CYT-103 monoclonal antibody requires selection of an antibody capable of binding to an antigen that is over-expressed in an ovarian cancer (see page 820 under the heading "Patients, Materials, and Methods").

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

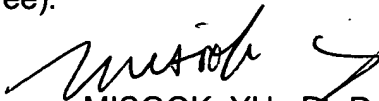
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


MISOOK YU, Ph.D
Examiner
Art Unit 1642

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: April 6, 2004, 14:05:54 ; Search time 17 Seconds
(without alignments)
1001.585 Million cell updates/sec

Title: US-09-787-844-2
Perfect score: 1792
Sequence: 1 RQRCGRQAGEANGARGAL.....PSNPLFPFLWALPLGPV 327

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 141661 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141661

Minimum DB seq length: 0
Maximum DB seq length: 2000000000
Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_42.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match %	Length	ID	Description
1	1728	96.4	314	1	TEST_HUMAN
2	1147	64.0	324	1	TEST_MOUSE
3	603	33.6	321	1	TRYG_HUMAN
4	580	32.4	343	1	PS68_HUMAN
5	574	32.0	290	1	PR27_HUMAN
6	562.5	31.4	342	1	PS88_RAT
7	561.5	31.3	342	1	PS88_MOUSE
8	556.5	31.1	311	1	TRYG_MOUSE
9	544	30.4	273	1	TRYT_SHEEP
10	543	30.3	811	1	TMS6_MOUSE
11	531.5	29.7	317	1	BSS4_HUMAN
12	528.5	29.5	270	1	TRYT_MERUN
13	522	29.1	275	1	TRYT_PIG
14	520	29.0	306	1	BSS4_MOUSE
15	515	28.7	275	1	TRB1_HUMAN
16	514.5	28.7	638	1	KAL_MOUSE
17	514	28.7	275	1	TRB2_HUMAN
18	513	28.6	638	1	KAL_MOUSE
19	512	28.6	276	1	MCT6_MOUSE
20	511	28.5	275	1	TRYT_CANFA
21	511	28.5	638	1	KAL_RAT
22	509.5	28.4	273	1	MCT7_RAT
23	509	28.4	811	1	TMS6_HUMAN
24	508.5	28.4	454	1	MCT3_HUMAN
25	507	28.3	273	1	MCT7_MOUSE
26	505	28.2	453	1	TMS3_MOUSE
27	500	27.9	274	1	MCT5_RAT
28	499	27.8	275	1	TRYA_HUMAN
29	490.5	27.4	435	1	TMS4_MOUSE
30	489.5	27.3	418	1	HATT_HUMAN
31	487.5	27.2	455	1	TMS5_MOUSE
32	483.5	27.0	625	1	FAIL_HUMAN
33	478	26.7	437	1	TMS4_HUMAN

RESULT 1
ID TEST_HUMAN STANDARD; PRT; 314 AA.
AC Q9Y6M0; Q9NS34; Q9P2V6;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 15-MAR-2004 (Rel. 43, Last annotation update)
DE Testisin precursor (EC 3.4.21.-) (Eosinophil serine protease 1) (ESP-1) (UNQ266/PRO303)
DE 1) (UNQ266/PRO303)
OS Homo sapiens (Human)
OS Homo sapiens (Human)
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A. (ISOFORM 1).
RC TISUS-Eosinophil;
RX MEDLINE=99045401; PubMed=9826525;
RA Inoue M., Kanbe N., Kuroiwa M., Kido H.;
RT "Cloning and tissue distribution of a novel serine protease esp-1 from human eosinophils";
RL Biochem. Biophys. Res. Commun. 252:307-312(1998).
[2]
RP SEQUENCE FROM N.A. (ISOFORM 3).
RX MEDLINE=2006805; PubMed=1060542;
RA Inoue M., Inoue M., Itoyama T., Kido H.;
RT "Structural analysis of esp-1 gene (PRSS 21)";
RL Biochem. Biophys. Res. Commun. 266:564-568(1999).
[3]
RP SEQUENCE FROM N.A. (ISOFORMS 1 AND 2).
RC TISUS-Cervical carcinoma;
RX MEDLINE=99323395; PubMed=10397266;
RA Hooper J.D., Nicol D.L., Dickinson J.L., Byre H.J., Scarman A.B., Norwyle J.F., Stutgen M.A., Douglas M.L., Loveland K.A., Sutherland G.R., Antalis T.M.;
RT "Testisin, a new human serine proteinase expressed by premalignant testicular germ cells and lost in testicular germ cell tumors";
RL Cancer Res. 59:3199-3205(1999).
[4]
RP SEQUENCE FROM N.A.
RX MEDLINE=40461760; PubMed=11004480;
RA Hooper J.D., Bowen N., Marshall H., Cullen L.M., Sood R., Daniels R., Stutgen M.A., Norwyle J.F., Higgs D.R., Kastner D.L., Ogbourne S.M., Pera M.F., Jazwinska E.C., Antalis T.M.;
RT "Localization, expression and genomic structure of the gene encoding the human serine proteinase testisin";
RL Biochim. Biophys. Acta 1492:63-71(2000).
[5]
RP SEQUENCE FROM N.A. (ISOFORM 1).
RX MEDLINE=42887296; PubMed=12975309;
RA Clark H.P., Gurney A.L., Abaya E., Baker K., Baldwin D., Brush J., Chen J., Chow B., Chui C., Crowley C., Currell B., Deuel B., Dowd P., Eaton D., Foster J., Grimaldi C., Gu Q., Hase P.E., Heldens S., Huang A., Kim H.S., Klimowski L., Jin Y., Johnson S., Lee J., Lewis L., Liao D., Mark M., Robbie S., Sanchez C., Schoenfeld J., Seshagiri S., Simmons L., Singh J., Smith V., Stinson J., Vagta A.,

ALIGNMENTS

34	477.5	26.6	417	1	HEPS_HUMAN
35	472.5	26.4	422	1	DESI_HUMAN
36	468	26.1	430	1	TMS2_MOUSE
37	466	26.0	436	1	HEPS_MOUSE
38	459.5	25.6	432	1	TMS2_HUMAN
39	457.5	25.5	457	1	TMS5_HUMAN
40	455.5	25.4	415	1	ACRO_PIG
41	455.5	25.4	810	1	PLAN_HUMAN
42	454.5	25.4	1069	1	ENTK_MOUSE
43	454	25.3	338	1	PLAN_HORSE
44	452.5	25.3	436	1	ACRO_MOUSE
45	447	24.9	416	1	HEPS_RAT

P05981	homo sapien
Q91522	homo sapien
Q91498	mus musculus
O55453	mus musculus
O51993	homo sapien
Q9H363	homo sapien
P08001	sus scrofa
P00747	homo sapien
P97435	mus musculus
P80010	equus caball
P23578	mus musculus
Q05511	rattus norv

